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Octanol/Water Partition Coefficients and Aqueous Solubilities of Organic Compounds

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U.S. DEPARTMENT OF COMMERCE
National Bureau of Standards
Center for Chemical Physics
Chemical Thermodynamics Division
Washington, DC 20234

December 1981

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Aqueous solubilities and octanol/water partition coefficients of organic solutes, falling into 7 general chemical classes, have been systematically determined using the modified generator column method. From thermodynamics an equation is derived relating $K_{O/W}$ to the volume-fraction-based solute activity coefficient in water (γ_S^W), the latter being determinable from C_S^W. For each class of compounds, excellent linear correlations are found between log $K_{O/W}$ and log γ_S^W, with slopes close to the theoretical value of unity.

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DISCLAIMER

Certain commercial equipment, instruments, and materials are identified in this paper in order to specify adequately the experimental procedure. In no case does such identification imply recommendation or endorsement by the National Bureau of Standards, nor does it imply that the material, instruments, or equipment identified are necessarily the best available for the purpose.

I. SUMMARY

A chromatographic method for measuring the octanol/water partition coefficient, $K_{o/w}$, and the aqueous solubility, C_s^w, of hydrophobic substances is described. When water is pumped through generator columns containing a solid support coated with an organic stationary phase, an aqueous solution is generated which is in equilibrium with the stationary phase. When the organic phase is pure solute, the concentration of the solute in the eluted aqueous phase is the solute solubility. When the organic phase is octanol containing a solute of concentration C_s^o and the concentration of the solute in the aqueous phase is determined to be C_s^w, then the octanol/water partiton coefficient is given as $K_{o/w} = C_s^o/C_s^w$. Validation of the generator column method was made by comparing $K_{o/w}$ and C_s^w values of n-propylbenzene carefully measured by the conventional shake-flask method with those measured by the generator column method. Additional validation of the method was made by analyzing $K_{o/w}$ and C_s^w data measured by the generator column method in terms of the thermodynamically derived equation.

$$\log K_{o/w} = -\log \phi_s^w - \log \gamma_s^o$$

where γ_s^o is the solute activity coefficient, on a volume fraction basis, in octanol as measured by the GC method and ϕ_s^w is the solute volume fraction in water which is determined from C_s^w data.

Thermodynamic theory predicts that plots of $\log K_{o/w}$ versus $\log \frac{1}{\phi_s^w}$ should have slopes of unity if the data are accurate while the coefficient of determination gives precision of the measurements. Analysis of the data for 62 compounds representing seven chemical classes gave slopes in the range 0.93 to 1.08 with an average coefficient of determination 0.994.

Our studies indicate that the C_s^w and $K_{o/w}$ data obtained by using the generator column method agree very well with the shake-flask literature data obtained experimentally. Thus these results establish that the data are accurate and the generator column method is a valid method for measuring C_s^w and $K_{o/w}$.

II. INTRODUCTION

Measurement of the aqueous solubility, C_s^w, and the octanol/water partition coefficient, $K_{o/w}$, are important for determining the fate and transport of organic chemicals in the environment. $K_{o/w}$ may be considered as a quantitative measure of the hydrophobicity of the compound. In this respect, it has been used to predict bioconcentration of organic pollutants in trout muscle [Neely et al., 1974] and for making other chemical and biological correlations [Leo et al., 1971]. The aqueous solubility gives an insight into environmental movement and distribution and the potential for biodegradation by microorganisms in soil surfaces, water, and sewage treatment plants as well as other degradation pathways such as photolysis, hydrolysis, and oxidation.

Octanol/water partition coefficients and aqueous solubilities are often measured by a shake-flask method. Solubilities are determined by shaking the solute with water, allowing the two phases to separate, and then determining the solute concentration in the aqueous phase by an appropriate analytical technique. Octanol/water partition coefficients are determined by shaking a known volume of octanol containing a small amount of solute with water, allowing the two phases to separate, and measuring the solute concentration in the aqueous phase, C_s^w, and in the octanol phase, C_s^o . $K_{o/w}$ is determined as the ratio C_s^o/C_s^w.

In any shake-flask experiment with a hydrophobic substance, the solute concentration in the aqueous phase is low. Consequently the measurement of this concentration can be seriously affected by the presence of colloidal dispersions (emulsions), adsorption of the solute onto surfaces of transfer vessels, and loss of a volatile solute into the atmosphere. These errors can be reduced, but only at a cost of inconvenience and increased time, by centrifuging or

replacing the shaking by gentle stirring, by prerinsing the glassware with the aqueous phase, and by avoiding exposure of the aqueous phase to the atmosphere. A rapid, convenient method for preparing equilibrated aqueous phases without significant errors from such effects would be desirable.

For this purpose we have adapted the generator column method described by May et al. [1978]. A generator column has a solid support coated with a solid or liquid stationary phase. When water is pumped through the column, an aqueous solution is generated which is equilibrated with the stationary phase. May et al. [1973] used their generator columns, packed with glass beads, mainly to measure solubilities of solid polycyclic aromatic hydrocarbons; the only liquid stationary phase used by them was benzene [May et al., 1978]. We have redesigned the generator column, changed the support to silanized silica in order to increase the coverage, and extended the stationary phase to hydrocarbon-octanol mixtures.

In this report we discuss the work done under Interagency Agreement EPA-80-2095 in the period October 1, 1980 to September 30, 1981. The objective of this work was to develop and validate a chromatographic method to measure C_s^w and $K_{o/w}$ and to make measurements on selected classes of organic compounds in order to obtain accurate and precise $K_{o/w}$ and C_s^w values.

In the third section of this report, "Comparison of the Experimental Methods," the shake-flask method is compared with the generator column method. The advantages and limitations of both methods are discussed.

The fourth section includes experimental details of the generator column method and the gas-liquid chromatographic method for determination of activity coefficients and octanol/water partiton coefficients of organic compounds.

In the fifth section, "Direct Experimental Validation of the Generator Column Method," the work done to establish a bench-mark C_s^w and $K_{o/w}$ measurement for n-propylbenzene is discussed. A detailed error analysis investigating every experimental parameter was made in order to arrive at the best $K_{o/w}$ and C_s^w values. These values were then compared with the values measured by the shake-flask method.

In the sixth section, "Results and Discussion," $K_{o/w}$ and C_s^w values are given for over 90 compounds representing seven types of organic compounds. Further validation of the generator column method is made by analyzing the data using linear regression analysis to the thermodynamically derived equation $\log K_{o/w} = c \log \gamma_s^w + d$, where c and d are series constants and γ_s^w is the activity coefficient of solutes in water saturated with octanol. The accuracy and precision of the data is discussed in terms of the value of the slope, c, and the coefficient of determination, r^2, for the regression analysis of the data to the different chemical classes.

In the seventh section, "Recommendations for Future Work," we recommend that additional $K_{o/w}$ and C_s^w measurements be made in aqueous NaCl solutions and simulated sea water in order to establish the salinity dependence of these properties. We also recommend that C_s^w measurements be made at different temperatures in order to establish the temperature dependence of solubility and that solute activity coefficients be measured by a head-space method to further validate the generator column method. There is also a need for $K_{o/w}$ and C_s^w measurement on classes of compounds not studied in this report.

In Appendix I, the thermodynamic derivation is given for the correlating equation

$$\log K_{o/w} = - \log \phi_s^w - \log \gamma_s^o$$

where ϕ_s^w is the volume fraction of solute in water saturated with octanol and γ_s^o is the activity coefficient, on a volume fraction basis, of the

solute in octanol saturated with water.

Appendix II includes the proposed test method for determination of the aqueous solubility of organic compounds.

III. COMPARISON OF EXPERIMENTAL METHODS

Generator columns have several advantages over shake-flask methods for equilibrating water with a liquid organic phase. The flow rate of water through the column can be made slow enough to avoid colloidal dispersions, while the large interfacial area between the organic and aqueous phases allows rapid equilibration. When the column is part of a continuous and closed flow system, the system walls become equilibrated with the aqueous solution and errors from adsorption are avoided; also there is no exposure of the solution to the atmosphere, thus loss of volatile solutes is avoided. Only about 1 mL of the organic phase is sufficient to load the column, and the column will generate samples of the aqueous solution of whatever volume is needed for analysis until the organic phase has been stripped. Once a column has been loaded with a given organic phase, it is a simple matter to vary other parameters such as pH or salinity of the aqueous phase to determine these effects on the aqueous solubilities of organic compounds.

For compounds having relatively large aqueous solubilities (>1.0 M) and low $K_{o/w}$ values (<100), there is no particular advantage in the generator columm method over the shake-flask method, since colloidal dispersion and surface adsorption are no longer an experimental problem. However, the generator column method is still preferred because it is more convenient to thermostat a generator column than a flask that must be shaken. The generator column method requires no special skill of the operator. The generator column is easy and inexpensive to construct and generally yields reproducible and accurate data at desired temperatures; whereas, one will require a thermostated centrifuge to obtain accurate results using the shake-flask method.

In summary, the generator column method is much better than the shake-flask method in that the measurement time is much less than the shake-flask method. Although equipment is required to measure the solute concentration in the two phases (HPLC or GLC) the generator column method with its closed flow system makes the measurements more convenient and avoids the intrinsic errors associated with the shake-flask method.

IV. EXPERIMENTAL

A. Aqueous solubility and partition coefficients

Reagents

The compounds (solutes) for which aqueous solubilities and octanol/water partition coefficients ($K_{o/w}$'s) were measured were obtained from various commercial sources with purities >98%. The octanol was purified by washing successively with 0.1 M H_2SO_4, 0.1 M NaOH, and distilled water. It was then dried with $CaCl_2$, filtered and distilled at atmospheric pressure. HPLC grade methanol and water were used to prepare the mobile phases for liquid chromatography. Ordinary distilled water was used for the aqueous phase solutions. Octanol saturated with water (w-octanol) was used for making up the solute in octanol solution. This solution was made up by stirring 10 mL of water with 250 mL of octanol for several hours. The lower excess water layer was removed by a siphon. For the $K_{o/w}$ measurements, a 1% (by weight) solute in w-octanol was used for coating the solid support in the generator column.

The design of the generator column and the method used to determine the solute concentration, C_s^w, in the aqueous phase depended on whether the solute absorbed the U.V. For compounds which absorbed in the U.V., high pressure liquid chromatography, HPLC, was used to determine C_s^w; for compounds which did not absorb in the U.V., solvent extraction followed by gas chromatographic analysis was used to determine C_s^w.

Generator Colum

The design of the generator column is shown in Figure 1. The column consists of a 6 mm (outside diameter) Pyrex tube joined to a short enlarged section of 9 mm Pyrex tubing. To pack the column a plug of silanized glass wool was inserted at one end of the 6 mm tube. Silanized diatomaceous silica support (about 0.5g 100-120 mesh Chromosorb W cleaned by Soxhlet extraction with ethanol and dried) was poured into the tube with tapping and retained with a second plug of silanized glass wool.

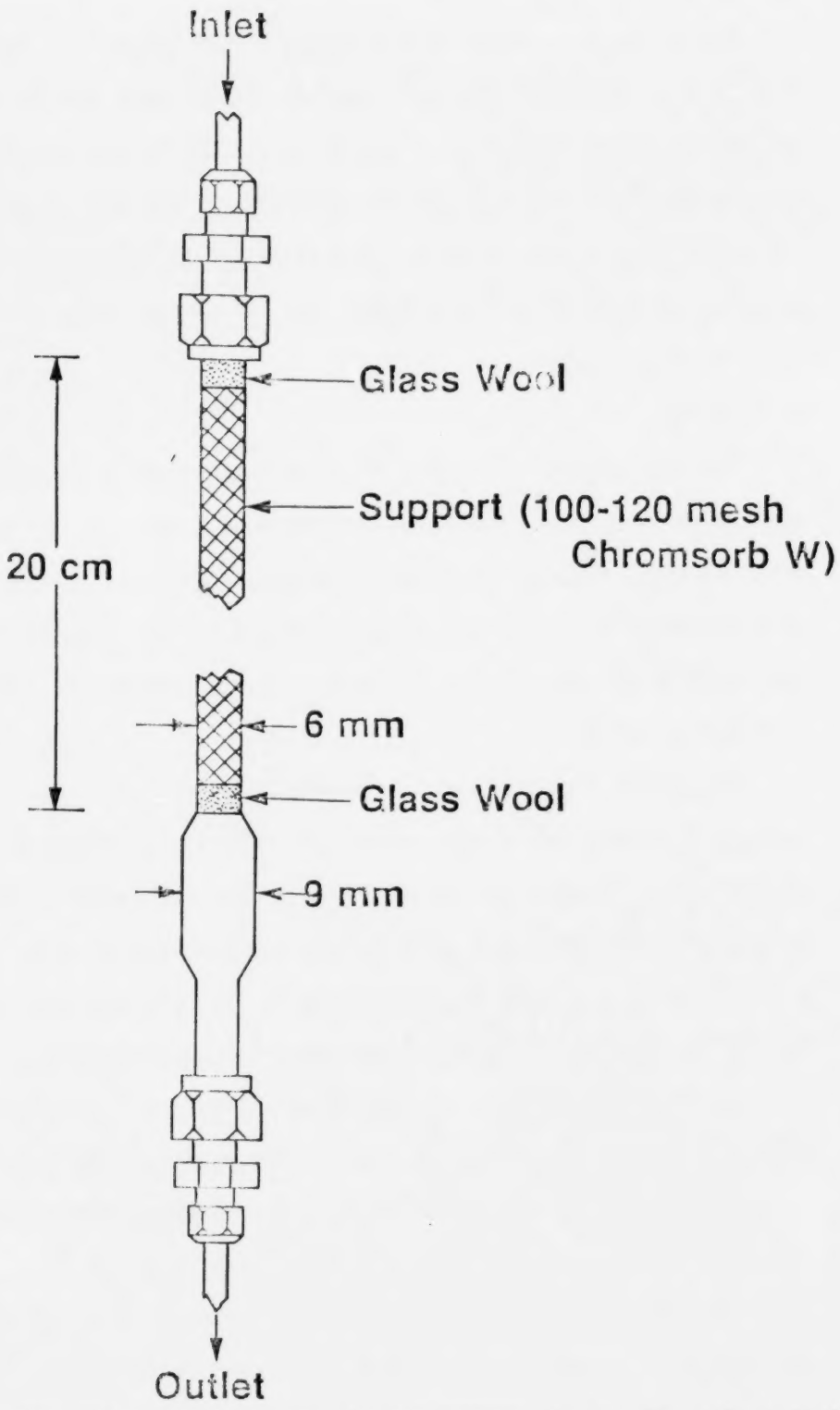

Figure 1. Generator column used to generate the aqueous phase. The column is 20 cm. long and packed with 100-120 mesh Chromosorb W for the solid support.

The column was coated with a liquid solute by pulling approximately 2 mL of the liquid through the clean dry support with gentle suction. The column was coated with a solid solute by dissolving the solute in a volatile solvent (10% v/v) and then pouring the mixture into the column until all the solid support was saturated as evident by the appearance of the volatile solution at the base of the column. The solvent was then distilled off under reduced pressure.

HPLC Method

The HPLC analytical system is shown schematically in Figure 2. Two reciprocating piston pumps delivered the mobile phase (water or a methanol-water mixture) through two 6-port high pressure rotary valves and a 30 X 0.6 cm C-18 analytical column to an ultraviolet absorption detector operating at 254 nm. Chromatogram peaks were recorded and integrated with a recording integrator.

One of the 6-port valves was sample injection valve used for injecting samples of either the octanol phase for analysis, or standard solutions of the solute in methanol for determining response factors. The sample loop volume was determined by a spectrophotometric method using basic chromate solution which are known to be suitable as absorption standards [Edisbury, 1967]. The method consisted of measuring the absorbance at 373 nm of three loopfuls of an aqueous stock solution of K_2CrO_4 (1.3% by weight) diluted to 50 mL with 0.2 percent KOH, and measuring the absorbance of the same stock solution after diluting 1:500 with 0.2 percent KOH. From these absorbances the loop volume was calculated to be (35.7 ± 0.1) mL.

The other 6-port valve in the system served as a switching valve for the extractor column which was used to remove solute from the aqueous solutions. The extractor column was a 6.6 X 0.6 cm stainless steel tube

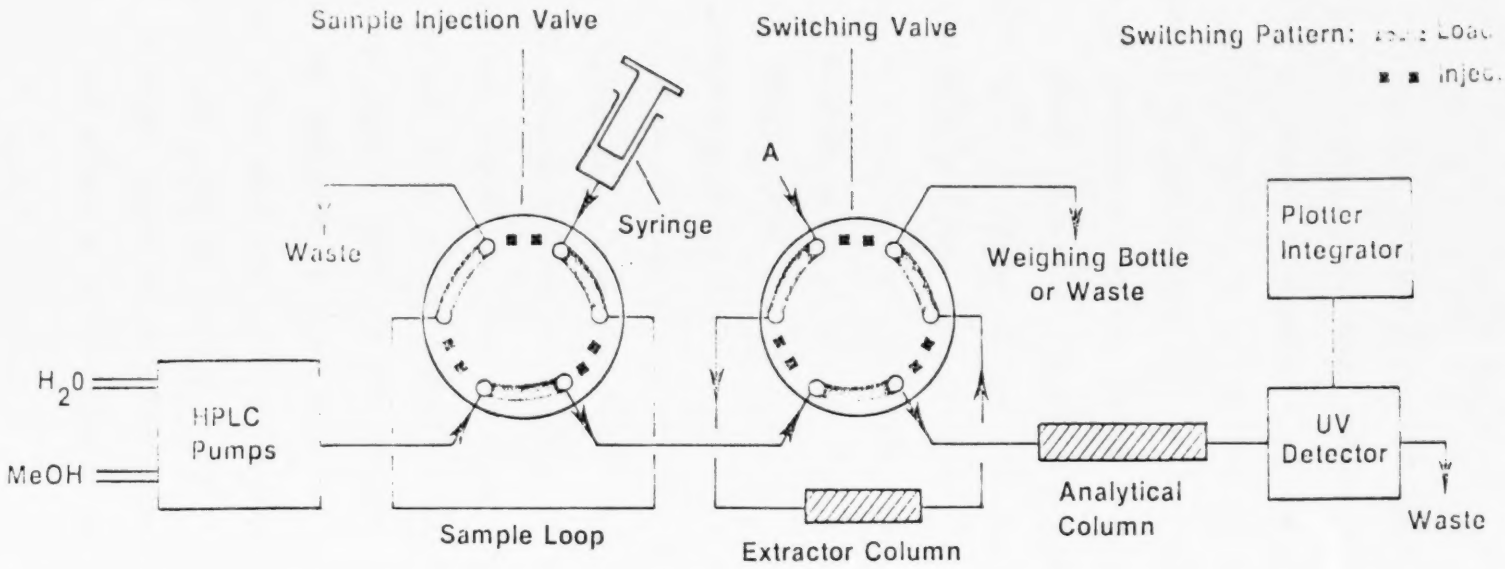

Figure 2. Schematic of the HPLC analysis system. The generator column outlet is connected at A and when a known amount of aqueous phase is collected in the weighing bottle, the switching valve is switched and the HPLC pumps transfer the mobile phase through the extractor column and into the analytical column. The syringe injection is used for calibration of the UV detector.

with stainless steel end fittings containing 5-μm frits, filled with a superficially porous reverse phase packing (Bondapak C_{18}/Corasil, Waters Associates). Aqueous solution from a generator column entered the switching valve through the 1/16 in (1.6 mm) stainless steel tubing labelled "A" in Figure 2. A water bath was used to thermostat to $\pm$ 0.05°C the generator column, the switching valve, the extractor column, and the interconnecting stainless steel tubing.

The procedure for analyzing the aqueous phase was first to flow the aqueous solution to waste with the switching valve in the inject position in order to equilibrate internal surfaces with the solution, thus insuring that the analyzed sample would not be depleted by solute adsorption on surfaces upstream from the valve. At the same time, water was pumped from the HPLC pumps in order to displace methanol from the extractor column. The switching valve was next changed to the load position to divert a sample of the solution through the extractor column, and the liquid leaving this column was collected in a weighing bottle. During this extraction step, the mobile phase was changed to a methanol-water mixture to condition the analytical column. After the desired volume of sample had been extracted, the switching valve was returned to the inject position for elution and analysis. Provided that there was no breakthrough of solute from the extractor column during the extraction step, the chromatographic peak represented all of the solute in the sample. The solute concentration in the aqueous phase was calculated from the peak area and the weight of the extracted liquid collected in the weighing bottle.

The octanol/water partition coefficient was calculated from the solute concentration in the octanol and aqueous phases by dividing the concentration in the octanol phase by the concentration in the aqueous phase. The water flow through the generator column was 2 mL/min. Further experiments with a generator column at 25°C show that within experimental error (standard deviation 3% or less) the measured aqueous concentration was independent of flow rate (in the range 0.5-2 mL/min).

GC Method

In the GC method aqueous solutions from the generator column entered a collecting vessel (Figure 3) containing a known weight of extracting solvent which was immiscible in water. The outlet of the generator column was positioned such that the aqueous phase always entered below the extracting solvent. After the aqueous phase was collected, the collecting vessel was stoppered with a 3/8" Teflon Swagelok cap, and the quantity of aqueous phase was determined by weighing. The solvent and the aqueous phase were equilibrated by either stirring with a glass enclosed magnet or by rotating the collecting vessel at the rate of two revolutions per minute for five minutes. It was found that rotating the collecting vessel for longer than five minutes did not increase the amount of solute extracted into the extracting solvent. A small amount of the solvent was then injected into a gas chromatograph equipped with flame ionization detector, and the solvent concentration in aqueous phase was determined from a calibration curve constructed using known concentrations of the solute. In order to determine the partition coefficient, $K_{o/w}$, samples of the 1% (by weight) solute in n-octanol solution were injected into the GC, and concentration of the solute in the octanol phase was similarly calculated from a calibration curve. As for the HPLC method, our experimental error in the GC method was less than 3%.

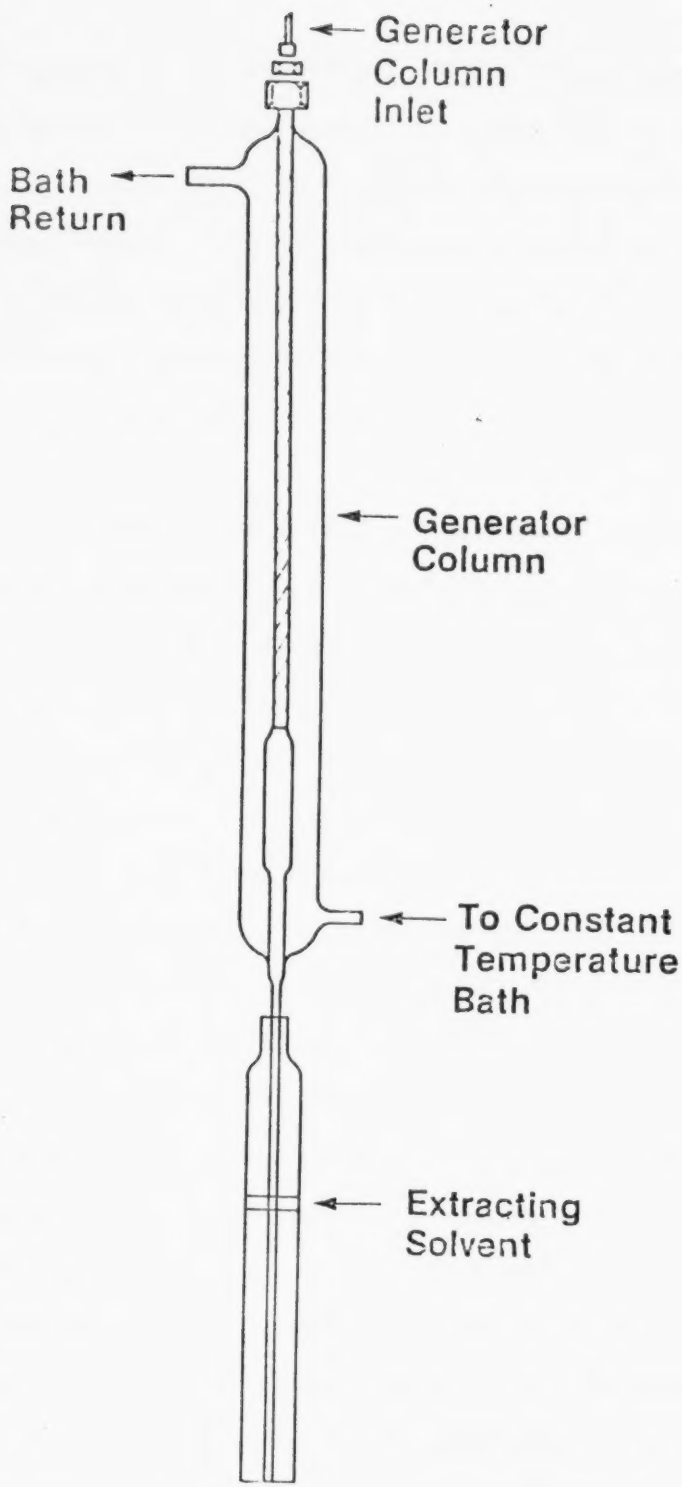

Figure 3. Generator column and collecting vessel used for analysis of the aqueous phase by the GC-solvent extraction method.

B. Solute activity coefficient in octanol

The stationary phase in octanol, was coated onto the support material, Chromosorb W-HP, 100/120 mesh, and the weight percent of coating was determined by an ashing method. A stainless steel column (1/8" OD) was then packed with a known amount of the coated support and was connected to a Hewlett-Packard 5830A gas chromatograph equipped with a flame ionization detector (FID) for the determination of the solute retention time. The temperature of the column was controlled by circulating water through a copper tubing jacket around the column and by a Haake Model FK temperature regulator which regulated the water temperature to 25.0 $\pm$ 0.05 °C.

The column inlet pressure, measured with a precalibrated pressure gauge (range 0-15 PSI), was kept constant during a run by regulating with a precision valve. In order to measure the carrier gas flow rate the column was disconnected from the FID, just before and after the experiment, and a soap bubble flowmeter was connected to the column outlet. The carrier gas was presaturated with n-octanol in order to reduce bleeding of the stationary phase.

Since the retention times decreased as the experiment progressed due to column loss of the n-octanol, toluene was used as a reference retention time standard and injected with each solute. The measured retention times were then corrected for bleeding using the reference solute retention time.

The solute specific retention volumes (V_g) were calculated by using the following equation

$$V_g = \frac{t_R \cdot F}{w} \cdot \frac{P_a - P_w}{P_a} \cdot \frac{273.2}{T_a} \cdot \frac{3}{2} \cdot \frac{(P_i/P_a)^2 - 1}{(P_i/P_a)^3 - 1}$$

where t_R is the retention time (minutes), F is the carrier gas flow rate (ml/min), P_i and P_a are the column inlet and atmospheric pressure (in Torr), P_w is the saturated water vapor pressure (in Torr) at room temperature T_a(^oK), and W is the weight (in gram) of stationary phase packed in the column. The solute activity coefficients at infinite dilution (γ_s^o) were determined from the following equation

$$\ln \gamma_s^o = \ln \frac{273.2Rd}{P_s V_g V_s} - \frac{P_s B_s}{RT}$$

where d is the density of n-octanol at 25.0°C, P_s and B_s are, respectively, the vapor pressure and the gas phase second virial coefficient of the pure solute at temeperature T(°K), R is the gas constant, and V_s is the molar volume of the solute at temperature T. Calculation of these quantities has been described in detail in our recent publication [Tewari et al., in press]. The estimated uncertainty in the activity coefficients is about 2%. However, we emphasize that the applicability of this technique is limited to only a few compounds due to the volatility of n-octanol. This technique can not be applied to those compounds which have 1mm or lower vapor pressure at 25.0°C.

V. VALIDATION

Because of the general lack of agreement in reported C_s^w and $K_{o/w}$ values, the first steps toward validation of the generator column method was to compare generator column data with data measured in this laboratory by the shake-flask method. Propylbenzene was chosen as the compound to establish a bench mark measurement because it is very stable, absorbs in the U.V., has a typical log $K_{o/w}$ and log C_s^w value, and can be obtained pure (>99.9 %) from commercial sources.

A. Shake-Flask Equilibrations

For each equilibration about 10 mL of water and about 4 mL of the organic phase were placed in a closed Pyrex vessel and stirred with a glass enclosed stirring bar. For the solubility measurements the organic phase was the pure solute. For the $K_{o/w}$ measurements the organic phase was a 1% (by weight) octanol solution. All precautions were taken to eliminate systematic error. All transfer vessels and tubing were prerinsed with the aqueous phase to avoid solute adsorption on the walls. The equilibration flask was stoppered at all times to avoid exposing the aqueous phase to the atmosphere. To prevent emulsion formation in the aqueous phase vigorous stirring was avoided. Most of the organic layer was confined to a narrow neck at the top of the vessel. Above the neck was a 3/8-inch tube septum for sampling the organic layer. The equilibrated aqueous phase was transferred to the HPLC system for analysis with the aid of nitrogen pressure.

B. Solubility

Table 1 lists our solubility results for propylbenzene. The aqueous samples were 2-6 mL in volume. The shake-flask and generator column results for comparable temperatures agree within experimental uncertainty. Our value at 25°C, 4.3×10^{-4} M, is similar to the values for this temperature reported by Andrews and Keefer [1950] (4.6×10^{-4} M) and by Hermann [1972] (5.0×10^{-4} M). The temperature dependence of the solubility suggests that there is a minimum in the neighborhood of 20°C. Solubility minima near 18°C have been observed for benzene and its methyl, dimethyl, and ethyl derivatives [Bohon and Claussen, 1951]. In the case of propylbenzene, Gill et al. [1976] predict from the temperature dependence of the heat of solution that there is a solubility minimum at (18.6 ± 0.2) °C which is consistent with our results.

C. Partition Coefficient

The octanol-water partition coefficient, $K_{o/w}$, was calculated from the measured propylbenzene concentrations in the equilibrated octanol and aqueous phases by dividing the concentration in the octanol phase by the concentration in the aqueous phase.

The volumes of the aqueous phase samples used to obtain the partition coefficient values listed in Table 2 were in the range 1-4 mL for the shake-flask results and 10-24 mL for the generator column results. The water flow rate through the generator columns was 2 mL/min. Further experiments with a generator column at 25°C showed that within experimental uncertainty (standard deviation 3% or less) the measured aqueous concentration was independent of the water flow rate (in the range 0.5-2 mL/min) and was independent of the volume of sample passed through the extractor column (in the range 2-24 mL). These experiments show that under our experimental conditions the equilibration was complete in the

Table 1

Aqueous Solubility of n-Propylbenzene

t/°C[a]	n[b]	C_s^w, 10^{-4} M[c]
stir-flask, stirred 16 h		
ambient	4	4.27 ± 0.06
Generator column		
15.0	3	4.26 ± 0.05
20.0	2	4.25 ± 0.12
25.0	3	4.32 ± 0.02
30.0	3	4.45 ± 0.05

[a]Equilibration temperature. Ambient is (23 ± 1)°C.

[b]Number of aqueous solution samples analyzed.

[c]Aqueous concentration; the mean value and the confidence limits at a 95% confidence level are listed.

Table 2

Octanol/Water Partition Coefficient, $K_{o/w}$, of n-Propylbenzene

Method Used	Conc. of propyl-benzene in octanol (Moles/liter)	Equilibrium Temperature (°C)	Number of Hours Stirred	Number of Octanol Phase samples Analyzed	Number of Aqueous Phase Samples Analyzed	Log $K_{o/w}$
Stir-flask	0.222	23 ± 1	24	4	4	3.73 ± 0.02
	0.223	23 ± 1	41	4	3	3.72 ± 0.01
	0.220	23 ± 1	44	3	4	3.71 ± 0.01
Generator column	0.038	25.0	-	4	9	3.69 ± 0.01
	0.086	25.0	-	4	4	3.70 ± 0.01
	0.223	25.0	-	4	6	3.72 ± 0.01
	0.223	10.0	-	4	2	3.71 ± 0.01
	0.223	15.0	-	4	2	3.72 ± 0.01
	0.223	20.0	-	4	2	3.74 ± 0.01
	0.223	30.0	-	4	4	3.72 ± 0.01
	0.223	35.0	-	4	3	3.68 ± 0.01

generator column, and that there was no significant breakthrough of propylbenzene from the extractor column.

Three shake-flask equilibrations with different stirring times were carried out (Table 2). With increased stirring time, there was a decrease in the partition coefficient values of about the same size as the experimental uncertainty. There is good agreement between these values and the generator column results.

The partition coefficient is seen to vary with temperature (Table 2) having a maximum in the vicinity of 20°C. However, further studies are required to generalize this phenomenon. It is interesting to note that while the solubility and the partition coefficient of propylbenzene both vary with temperature, their product over the temperature range in which both quantities were measured (15-30°C) is essentially constant (2.26 $\pm$ 0.05 M). This suggests that the heat of solution of propylbenzene in octanol is small.

The partition coefficient measurements at 25°C (Table 2) show a small but systematic decrease of log $K_{O/W}$ with decreasing concentration in the octanol phase. Extrapolation to infinite dilution gives log $K_{O/W}$ = 3.69 $\pm$ 0.01 at 25°C. Iwasa *et al.* [1965] report log $K_{O/W}$ = 3.68 $\pm$ 0.01 from shake-flask measurements at ambient temperature, in excellent agreement with our results.

Activity Coefficients

In Appendix I an expression is derived showing the relationship of log $K_{O/W}$ with the aqueous solubility in term of solute volume fraction ϕ_S^W

$$\log K_{O/W} = - \log \phi_S^W - \log \gamma_S^O$$

where ϕ_S^W is the solute volume fraction in water saturated with octanol

and γ_s^o is the solute activity coefficient, on a volume fraction basis, in octanol saturated with water. This equation provides an indirect method to determine $K_{o/w}$ from the solute activity coefficient in octanol and its aqueous solubility.

The solute activity coefficient in octanol, γ_s^o , can be determined from the retention volume [Conder and Young, 1979] of the solute eluting from a G.C. column containing octanol saturated with water as the stationary phase. This method for determination of $K_{o/w}$ has been documented in our recent publication [Tewari et al., in press]. Since γ_s^o is measured at infinite dilution and ϕ_s^w is also at infinite dilution, the $K_{o/w}$ determined using the above equation is also at infinite dilution.

The value for log γ_s^o determined by the G.C. method for a number of solutes are listed in Table 3. Using γ_s^o and γ_s^w determined from the aqueous solubility and solute molar volume, octanol/water partition coefficients for the solutes were calculated and compared with the experimental $K_{o/w}$. These two quantities are listed in the last two columns of table 3. An examination of these two columns shows an excellent agreement between the experimental $K_{o/w}$ and the calculated $K_{o/w}$. Based on our measurements, there is a complete consistency in the above equation. Thus these results suggest that our data are precise and accurate and that the generator column is a valid method for determination of the aqueous solubility and octanol/water partition coefficient of organic compounds.

In conclusion, we have demonstrated in this section that the generator column method for determining C_s^w and $K_{o/w}$ is a valid and an accurate method for measuring these quantities.

Table 3

Activity Coefficients and Octanol/Water Partition Coefficients of Organic Compounds at 25.0°C

Solutes	$\log \gamma_s^o$	$\log \gamma_s^w$	$\log K_{o/w}$	
	(GLC)		Calculated	Experimental
Benzene	0.565	2.59	2.03	2.13
Toluene	0.509	3.17	2.66	2.65
Ethylbenzene	0.506	3.66	3.15	3.13
o-Xylene	0.494	3.60	3.11	3.13
m-Xylene	0.477	3.73	3.25	3.20
Chlorobenzene	0.533	3.36	2.83	2.81
n-Propylbenzene	0.494	4.22	3.73	3.69
n-Pentane	0.555	4.19	3.64	3.62
n-Hexane	0.530	4.73	4.20	4.11
n-Heptane	0.517	5.28	4.76	4.66
n-Octane	0.513	5.80	5.29	5.18
Ethyl acetate	0.621	1.15	0.53	0.68
n-Propylacetate	0.534	1.64	1.11	1.24
n-Butylacetate	0.425	2.12	1.69	1.82
3-Pentanone	0.496	1.25	0.75	0.99
2-Heptanone	0.222	2.30	2.08	1.98
1-Hexene	0.504	3.98	3.47	3.47
1-Octene	0.479	5.24	4.76	4.88
1-Nonene	0.469	5.81	5.34	5.35
n-Butylbromide	0.372	3.16	2.79	2.75
1-Butanol	0.336	1.10	0.76	0.79

VI. RESULTS AND DISCUSSION

The experimentally determined values of $K_{o/w}$ and C_s^w and the calculated values of γ_s^w are listed in Tables 4 through 10 for several classes of compounds. The notations a and b refer, respectively, to the HPLC and GC methods of analysis. The average experimental uncertainties in $K_{o/w}$ and C_s^w are around 1.0%. An asterisk is used to indicate that the literature data are calculated values according to Hansch et al. (1968). Our results are generally in good agreement with available experimental literature data obtained by the conventional shake-flask method.

The present data were subjected to a linear regression of $\log K_{o/w} = c \log \gamma_s^w + d$ for each class of compound and for all compounds taken together. The results of these analyses are shown in Table 11.

The present equations are inadequate to explain $K_{o/w}$ and C_s^w data of aromatic solids listed in Table 4A. Analysis of these data is, therefore, not included in Table 11.

According to equation 9 of Appendix I the slope for each class should be unity and the negative of the intercept is $\log \gamma_s^o$ (assumed to be relatively constant). Examination of Table 11 shows that the slopes are indeed close to unity, ranging between 0.91 and 1.08. These small deviations are most likely caused by slight variations in $\log \gamma_s^o$ within each class (Tewari et al., in press). For example, the average of the difference between $\log \gamma_s^w$ and $\log K_{o/w}$ for the aromatic compounds is 0.55 for those with aliphatic substituents and 0.68 for those with halogen substituents, whereas the least-squares value of $\log \gamma_s^o$ is 0.77 when all the aromatic compounds are included. Therefore, the intercepts represent only approximate (averaged) values of $\log \gamma_s^o$ for each class.

These findings show that the octanol/water partition coefficient of a solute may be estimated with reasonable accuracy from knowledge of its aqueous

Table 4

AQUEOUS SOLUBILITIES AND OCTANOL/WATER PARTITION

COEFFICIENTS OF ORGANIC COMPOUNDS

Solute	Aqueous Concentration		$\log \gamma_s^{w(i)}$	$\log K_{o/w}$
	This Study (M)	Literature Value (M)		This Study[j] / Literature
Aromatic Hydrocarbons				
Toluene	6.28×10^{-3}	5.80×10^{-3}[c]	3.17	2.65[a] / 2.69[f]
Ethylbenzene	1.76×10^{-3}[a]	1.52×10^{-3}[c]	3.66	3.13[a] / 3.15[f]
o-Xylene	2.08×10^{-3}	1.61×10^{-3}[c]	3.60	3.13[a] / 3.12[f]
m-Xylene	1.51×10^{-3}[a]	1.38×10^{-3}[c]	3.73	3.20[a] / 3.20[f]
p-Xylene	2.02×10^{-3}[a,b]	1.47×10^{-3}[c]	3.60	3.18[a,b] / 3.15[f]
n-Propylbenzene	4.34×10^{-4}[a,b]	4.99×10^{-4}[f]	4.22	3.69[a,b] / 3.68[f]
n-Butylbenzene	1.03×10^{-4}[a,b]	8.79×10^{-5}[c]	4.79	4.28[a,b] / 4.26[f]
m-Pentylbenzene	2.59×10^{-5}[a]	---	5.35	4.90[a] / ---
n-Hexylbenzene	6.27×10^{-6}[a]	---	5.92	5.52[a] / ---
1,2,3-Trimethyl benzene	5.45×10^{-4}[a]	4.01×10^{-4}[c]	4.13	3.55[a] / ---
1-Ethyl-2-methylbenzene	6.21×10^{-4}[a]	---	4.07	3.53[a] / ---
Chlorobenzene	2.62×10^{-3}[a]	2.84×10^{-3}[e]	3.56	2.98[a] / 2.84[f]
Bromobenzene	2.62×10^{-3}[e]	4.41×10^{-3}[e]	3.56	2.98[a] / 2.99[f]
Iodobenzene	9.84×10^{-4}[a]	---	3.96	3.28[a] / 3.25[f]
o-Fluorobenzyl chloride	2.88×10^{-3}[a]	---	3.47	2.67[a] / ---
m-Fluorobenzyl chloride	2.86×10^{-3}[a]	---	3.46	2.77[a] / ---
m-Cresol	2.59×10^{-2}[a]	---	2.52	1.96[a] / ---
Nitrobenzene	3.11×10^{-2}[a]	---	2.50	1.85[a] / ---

* Indicates that the literature data are calculated values according to Hansch et al., 1968.

(a) HPLC method of analysis.

(b) GC method of analysis.

(c) Sutton and Calder, 1975.

(d) McAuliffe, 1966.

(e) Hansch et al., 1968.

(f) Hansch and Leo, 1979.

(g) MacKay et al., 1980.

(h) Reddick and Burger, 1955.

(i) Average standard deviation of $\log \gamma_s^w$ measurements is 0.04.

(j) Average standard deviation of $\log K_{o/w}$ measurements is 0.04.

AQUEOUS SOLUBILITIES, AND OCTANOL/WATER PARTITION COEFFICIENTS,

OF ORGANIC COMPOUNDS

Miscellaneous Aromatic Compounds

Solute	Aqueous Concentration		$\log \gamma_s^{w(i)}$	Log $K_{o/w}$	
	This study (M)	Literature (M)		This Study[j]	Literature
n-Heptylbenzene	2.54×10^{-6}(a)	---	6.28	---	---
n-Octylbenzene	3.48×10^{-7}(a)	---	7.11	---	---
Hexamethylbenzene	1.45×10^{-6}(a)	---	---	4.61(a)	---
1,2,3,5-Tetramethyl-benzene	---	---	---	4.04(a)	---
Naphthalene	2.39×10^{-4}(a)	2.36×10^{-4}(g)	---	3.35(a)	3.37(f)
1-Methylnaphthalene	2.23×10^{-4}(a)	2.11×10^{-4}(g)	---	---	---
1-Ethylnaphthalene	7.41×10^{-5}(a)	6.40×10^{-5}(g)	---	---	---
1-Fluoronaphthalene	3.53×10^{-4}(a)	---	---	---	---
1-Chloronaphthalene	1.07×10^{-4}(a)	---	---	---	---
1-Bromonaphthalene	6.72×10^{-5}(a)	---	---	---	---
p-Fluorobenzyl chloride	---	---	---	2.73(a)	---
o-Dichlorobenzene	---	---	---	3.38(a)	3.38(f)
m-Dichlorobenzene	---	---	---	3.48(a)	3.38(f)
p-Dichlorobenzene	---	---	---	3.37(a)	3.38(f)
1,2,3-Trichlorobenzene	---	---	---	4.04(a)	---
1,2,4-Trimethylbenzene	---	---	---	3.63(a)	---
1,2,3,4-Tetramethyl benzene	---	---	---	3.98(a)	---
Phenol	0.813(a)	---	---	1.45(a)	---
2,5-Dimethylphenol	6.61×10^{-2}(a)	---	---	2.35(a)	---
2,4-Dimethylphenol	6.40×10^{-2}(a)	---	---	2.34(a)	---
2,6-Dimethylphenol	7.90×10^{-2}(a)	---	---	2.31(a)	---
2,3,6-Trimethyl phenol	1.16×10^{-2}(a)	---	---	2.67(a)	---
2,4,6-Trimethyl phenol	---	---	---	2.73(a)	---
o-Cresol	2.52×10^{-2}(a)	---	---	1.96(a)	---

(*) Indicates that the literature data are calculated values according to Hansch et al., 1968.

(a) HPLC method of analysis.

(b) GC method of analysis.

(c) Sutton and Calder, 1975.

(d) McAuliffe, 1966.

(e) Hansch et al., 1968.

(f) Hansch and Leo, 1979.

(g) MacKay et al., 1980.

(h) Reddick and Burger, 1955.

(i) Average standard deviation of log γ_s^w measurements is 0.05.

(j) Average standard deviation of log $K_{o/w}$ measurements is 0.04.

Table 5

AQUEOUS SOLUBILITIES AND OCTANOL/WATER PARTITION COEFFICIENTS OF ORGANIC COMPOUNDS

Solute	Aqueous Concentrations		log $\gamma_s^{w(i)}$	log $K_{o/w}$	
	This Study (M)	Literature value (M)		This Study[j]	Literature Value
Unsaturated Hydrocarbons					
1-Hexene	8.28×10^{-4}[b]	5.89×10^{4}[d]	3.98	3.47[b]	2.70[e]*
1-Heptene	1.85×10^{-4}[b]	---	4.58	3.99[b]	---
1-Octene	3.65×10^{-5}[b]	2.40×10^{-5}[d]	5.24	4.88[b]	3.70[e]*
1-Nonene	8.85×10^{-6}[b]	---	5.81	5.35[b]	---
1-Pentyne	1.54×10^{-2}[b]	---	2.81	2.12[b]	---
1-Hexyne	8.37×10^{-3}[b]	---	3.01	2.73[b]	---

* Indicates that the literature data are calculated values according to Hansch et al., 1968.

(a) HPLC method of analysis.

(b) GC method of analysis.

(c) Sutton and Calder, 1975.

(d) McAuliffe, 1966.

(e) Hansch et al., 1968.

(f) Hansch and Leo, 1979.

(g) MacKay et al., 1980.

(h) Reddick and Burger, 1955.

(i) Average standard deviation of log γ_s^w measurements is 0.05.

(j) Average standard deviation of log $K_{o/w}$ measurements is 0.04.

Table 6

AQUEOUS SOLUBILITIES AND OCTANOL/WATER PARTITION

COEFFICIENTS OF ORGANIC COMPOUNDS

Halogenated Hydrocarbons

Solute	Aqueous Concentration		Log $\gamma_S^{w(i)}$	log $K_{o/w}$	
	This Study (M)	Literature Value (M)		This Study[(j)]	Literature Value
1-Chlorobutane	9.43×10^{-3}[(b)]	7.19×10^{-3}[(e)]	3.00	2.55[(b)]	2.39[(e)]
1-Chloroheptane	1.01×10^{-4}[(b)]	---	4.81	4.15[(b)]	---
1-Bromobutane	6.34×10^{-3}[(b)]	4.13×10^{-3}[(e)]	3.16	2.75[(b)]	2.60[(e)]*
1-Bromopentane	8.38×10^{-4}[(b)]	---	3.98	3.49[(b)]	---
1-Bromohexane	1.56×10^{-4}[(b)]	---	4.65	3.80[(b)]	---
1-Bromoheptane	3.71×10^{-5}[(b)]	---	5.23	4.36[(b)]	---
1-Bromooctane	8.65×10^{-6}[(b)]	---	5.82	4.89[(b)]	---
Bromochloromethane	0.129[(b)]	---	2.06	1.41[(b)]	---
1-Bromo-2-chloro-propane	1.42×10^{-2}[(b)]	---	2.82	2.18[(b)]	---
1-Iodoheptane	1.55×10^{-2}[(b)]	---	5.60	4.70[(b)]	---
Trichloroethylene	1.04×10^{-2}	0.80×10^{-2}[(e)]	3.03	2.53[(a)]	---
4-Bromo-1-butene	5.66×10^{-3}	---	3.24	2.53[(a)]	---
Allyl bromide	3.17×10^{-2}	---	2.56	1.79[(a)]	---

* Indicates that the literature data are calculated values according to Hansch et al., 1968.

(a) HPLC method of analyis.

(b) GC method of analysis.

(c) Sutton and Calder, 1975.

(d) McAuliffe, 1966.

(e) Hansch et al., 1968.

(f) Hansch and Leo, 1979.

(g) MacKay et al., 1980.

(h) Reddick and Burger, 1955.

(i) Average standard deviation of log γ_S^w measurements is 0.03.

(j) Average standard deviation of log $K_{o/w}$ measurements is 0.03.

Table 7

AQUEOUS SOLUBILITIES AND OCTANOL/WATER PARTITION COEFFICIENTS OF ORGANIC COMPOUNDS

Normal Hydrocarbons

Solute	Aqueous Concentration		log $\gamma_s^{w(i)}$	log $K_{o/w}$	
	This Study (M)	Literature Value (M)		This Study[(j)]	Literature Value
n-Pentane	5.65×10^{-4}[(b)]	5.39×10^{-4}[(d)]	4.19	3.62[(b)]	3.23[(f)]
n-Hexane	1.43×10^{-4}[(b)]	1.13×10^{-4}[(d)]	4.73	4.11[(b)]	3.00[(e)]*
n-Heptane	3.57×10^{-5}[(b)]	$3.05 \times 10^{-}$[(d)]	5.28	4.66[(b)]	3.50[(e)]*
n-Octane	9.66×10^{-6}[(b)]	5.97×10^{-6}[(d)]	5.80	5.18[(b)]	4.00[(e)]*

* Indicates that the literature data are calculated values according to Hansch et al., 1968.

(a) HPLC method of analysis.

(b) GC method of analysis.

(c) Sutton and Calder, 1975.

(d) McAuliffe, 1966.

(e) Hansch et al., 1968.

(f) Hansch and Leo, 1979.

(g) MacKay et al., 1980.

(h) Reddick and Burger, 1955.

(i) Average standard deviation of log γ_s^w measurements is 0.06.

(j) Average standard deviation of log $K_{o/w}$ measurements is 0.02.

Table 8

AQUEOUS SOLUBILITIES AND OCTANOL/WATER PARTITION

COEFFICIENTS OF ORGANIC COMPOUNDS

Aldehydes and Ketones

Solute	Aqueous Concentrations		$\log \gamma_s^{w(i)}$	$\log K_{o/w}$	
	This Study (M)	Literature Value (M)		This Study[j]	Literature Value
2-Butanone	1.89[b]	---	0.77	0.69[b]	0.29[e]
3-Pentanone	0.53[b]	0.48[e]	1.25	0.99[b]	0.79[e]*
2-Heptanone	3.57×10^{-2}[a]	3.79×10^{-2}[e]	2.30	1.98[a]	1.79[e]*
2-Octanone	8.85×10^{-3}[a]	---	2.86	2.76[a]	---
2-Nonanone	2.61×10^{-3}[a]	---	3.35	3.18[a]	---
2-Decanone	5.03×10^{-4}[a]	---	4.02	3.81[a]	---
Acetal	0.75[b]	0.42[h]	0.97	0.52[a]	---
2-Furaldehyde	0.81	0.85[e]	1.17	.52[a]	---

* Indicates that the literature data are calculated values according to Hansch et al., 1968.

(a) HPLC method of analysis.

(b) GC method of analysis.

(c) Sutton and Calder, 1975.

(d) McAuliffe, 1966.

(e) Hansch et al., 1968.

(f) Hansch and Leo, 1979.

(g) MacKay et al., 1980.

(h) Reddick and Burger, 1955.

(i) Average standard deviation of log γ_s^w measurements is 0.05.

(j) Average standard deviation of log $K_{o/w}$ measurements is 0.03.

Table 9

AQUEOUS SOLUBILITIES AND OCTANOL/WATER PARTITION

COEFFICIENTS OF ORGANIC COMPOUNDS

Esters

Solute	Aqueous Concentrations		Log $\gamma_s^{w(i)}$	Log $K_{o/w}$	
	This Study (M)	Literature Value (M)		This Study[j]	Literature Value
Methyl nonanoate	1.33×10^{-4}[b]	---	4.58	4.32[b]	---
Methyl decanoate	2.05×10^{-5}[b]	----	5.36	4.41[b]	---
Ethyl acetate	0.726[b]	0.912[e]	1.15	0.68[b]	0.73[e]*
n-Propyl acetate	0.200[b]	0.185[e]	1.64	1.24[b]	1.23[e]*
n-Butyl acetate	5.77×10^{-2}[b]	0.203[e]	2.12	1.82[b]	1.73[e]*
Ethyl propionate	0.148	0.187[h]	1.77	1.43[b]	---
2-Bromoethyl acetate	0.212[a]	---	1.63	1.11[a]	---

* Indicates that the literature data are calculated values according to Hansch et al., 1968.

(a) HPLC method of analysis.

(b) GC method of analysis.

(c) Sutton and Calder, 1975.

(d) McAuliffe, 1966.

(e) Hansch et al., 1968.

(f) Hansch and Leo, 1979.

(g) MacKay et al., 1980.

(h) Reddick and Burger, 1955.

(i) Average standard deviation of log γ_s^w measurements is 0.04.

(j) Average standard deviation of log $K_{o/w}$ measurements is 0.02.

Table 10

AQUEOUS SOLUBILITIES AND OCTANOL/WATER PARTITION COEFFICIENTS OF ORGANIC COMPOUNDS

Alcohols

Solute	Aqueous Concentration		Log $\gamma_s^{w(i)}$	Log $K_{o/w}$	
	This Study (M)	Literature Value (M)		This Study[j]	Literature Value
1-Butanol	0.854[b]	---	1.0	0.785[b]	0.84[e]*
1-Pentanol	0.133[b]	0.249[h]	1.84	1.53[b]	1.34[f]*
1-Hexanol	4.14×10^{-2}[b]	---	2.28	2.03[b]	1.84[e]*
1-Heptanol	1.13×10^{-2}[b]	---	2.80	2.57[b]	2.34[e]*
1-Nonanol	7.35×10^{-4}[b]	---	3.89	3.77[b]	---
2 Ethyl-1,3-hexanediol	1.56×10^{-3}[b]	---	3.61	3.22[b]	---

* Indicates that the literature data are calculated values according to Hansch et al., 1968.

(a) HPLC method of analysis.

(b) GC method of analysis.

(c) Sutton and Calder, 1975.

(d) McAuliffe, 1966.

(e) Hansch et al., 1968.

(f) Hansch and Leo, 1979.

(g) MacKay et al., 1980.

(h) Reddick and Burger, 1955.

(i) Average standard deviation of log γ_s^w measurements is 0.03.

(j) Average standard deviation of log $K_{o/w}$ measurements is 0.03.

Table 11

Coefficients of the Regression Equation and

the Coefficient of Determination for the Solutes

Type of Compounds	Number of Compounds	Slope (c)	Intercept(d)	Coefficient of Determination (r^2)
Aromatic Hydrocarbons	18	1.056 ± 0.026	-0.768 ± 0.100	0.990
Unsaturated Hydrocarbons	6	1.024 ± 0.061	-0.585 ± 0.267	0.986
Halogenated Hydrocarbons	13	0.907 ± 0.033	-0.323 ± 0.133	0.986
Normal Hydrocarbons	4	0.972 ± 0.016	-0.468 ± 0.081	0.999
Aldehydes and Ketones	8	1.079 ± 0.065	-0.465 ± 0.155	0.978
Esters	7	0.932 ± 0.055	-0.285 ± 0.167	0.982
Alcohols	6	1.030 ± 0.011	-0.348 ± 0.112	0.994
All compounds	62	0.944 ± 0.018	-0.311 ± 0.066	0.980

solubility, its molar volume and the regression equation for compounds of its class. Also, this study establishes that the generator column method coupled with either HPLC or GC modes of analysis provides an accurate and rapid method for systematic determination of $K_{o/w}$ and C_s^w for organic compounds.

Equation 9 of Appendix I was rigorously derived from thermodynamic principles. Plots of log $K_{o/w}$ versus log γ_s^w having slopes of unity are a strong indication of the accuracy of the data. The scatter or precision of the data should be reflected in the coefficient of determination obtained from a linear regression analysis of the data. A coefficient near unity indicates good precision in the measurements.

The fact that the slopes of the log $K_{o/w}$ versus log γ_s^w plots for the seven different classes of compounds are near unity (Table 11) is a strong argument in favor of the generator column method giving accurate C_s^w and $K_{o/w}$ values and is a further validation of the method.

It is interesting to analyze literature values of $K_{o/w}$ and C_s^w in the same manner and compare these results with those obtained by the generator column method. In Figure 4 are plotted log $K_{o/w}$ values measured by the generator column against literature log $K_{o/w}$ values measured by the shake-flask method. The points that are obviously off in the literature log $K_{o/w}$ range of 2 to 4 are alkanes that have been calculated by the group additivity method and are not experimental values.

In Figure 5 are plotted log C_s^w values measured by the generator column method against literature log C_s^w values measured by the shake-flask method. The agreement is much better than that in Figure 5 because all the literature values are experimental values.

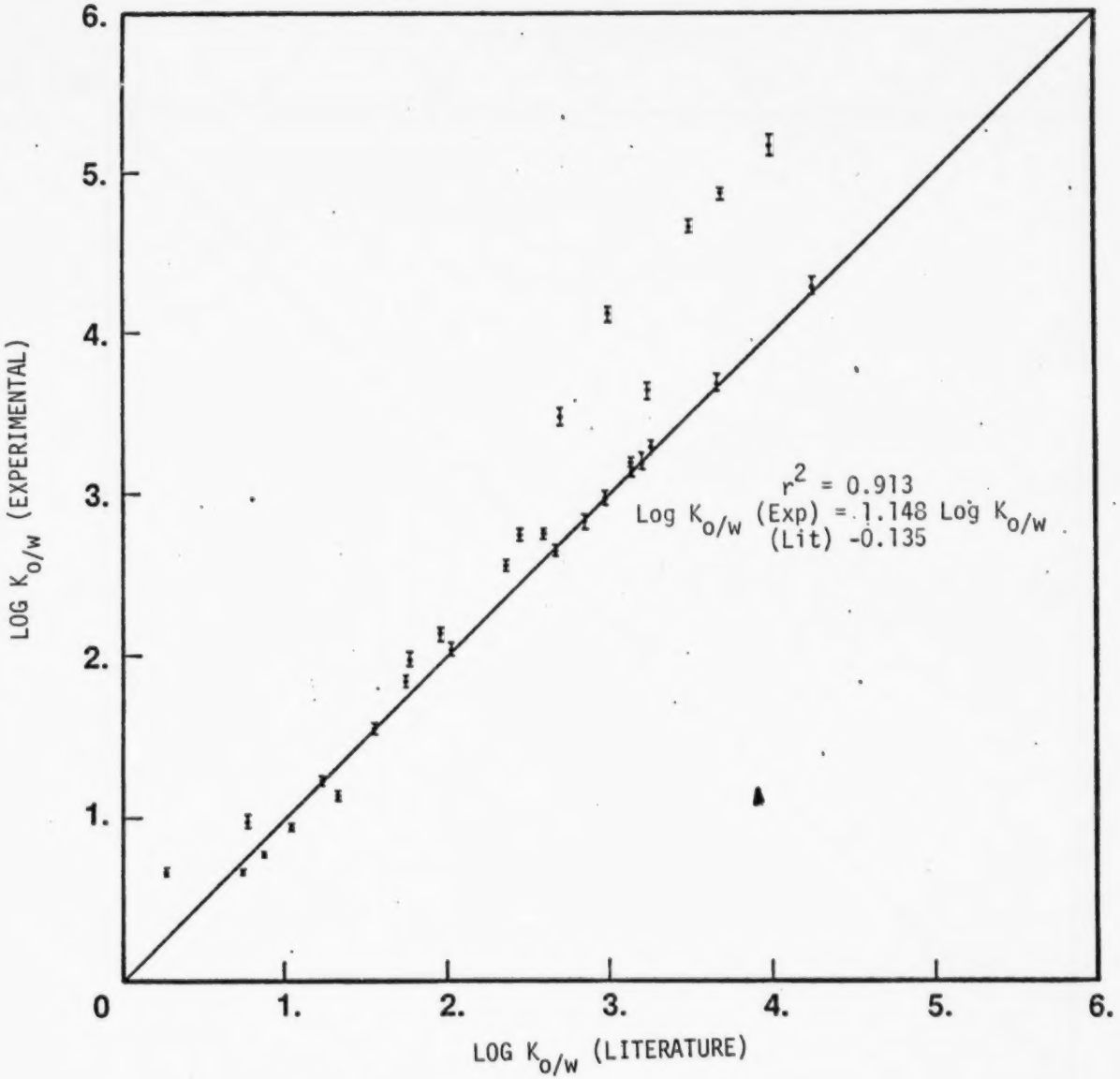

Figure 4. Experimental Log $K_{o/w}$ Versus Literature Log $K_{o/w}$.

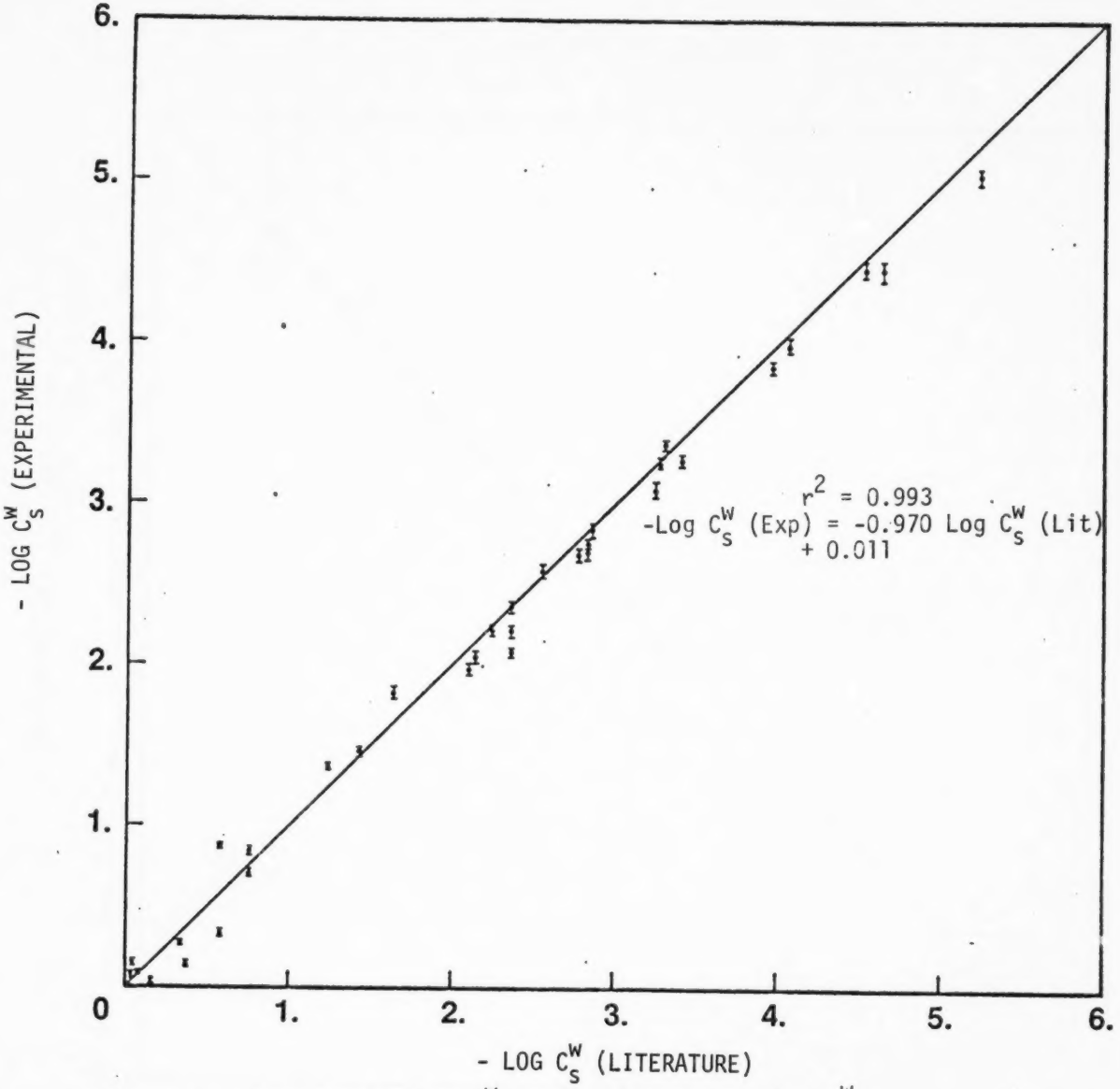

Figure 5. Experimental Log C_s^W Versus Literature Log C_s^W.

In Figure 6 are plotted literature log $K_{o/w}$ values versus literature log $1/C_s^w$ values. The large scatter in the points indicates the accuracy and/or the precision of the measurements is not very good. In Figure 7 are plotted log $K_{o/w}$ versus log $1/C_s^w$ where both $K_{o/w}$ and C_s^w were measured by the generator column method. The error bars indicate the precision of the measurements. A linear regression analysis of the data gives a slope of 0.994 with a coefficient of determination of 0.998 indicating that the measurements are accurate and precise.

In conclusion we feel that the Figures 4 through 7 and the regression analysis of the data on the seven different groups of compounds show that the slopes of the log $K_{o/w}$ versus log γ_s^w plots and the coefficients of determination of these plots are all approximately equal to unity. This is further validation of the generator column method.

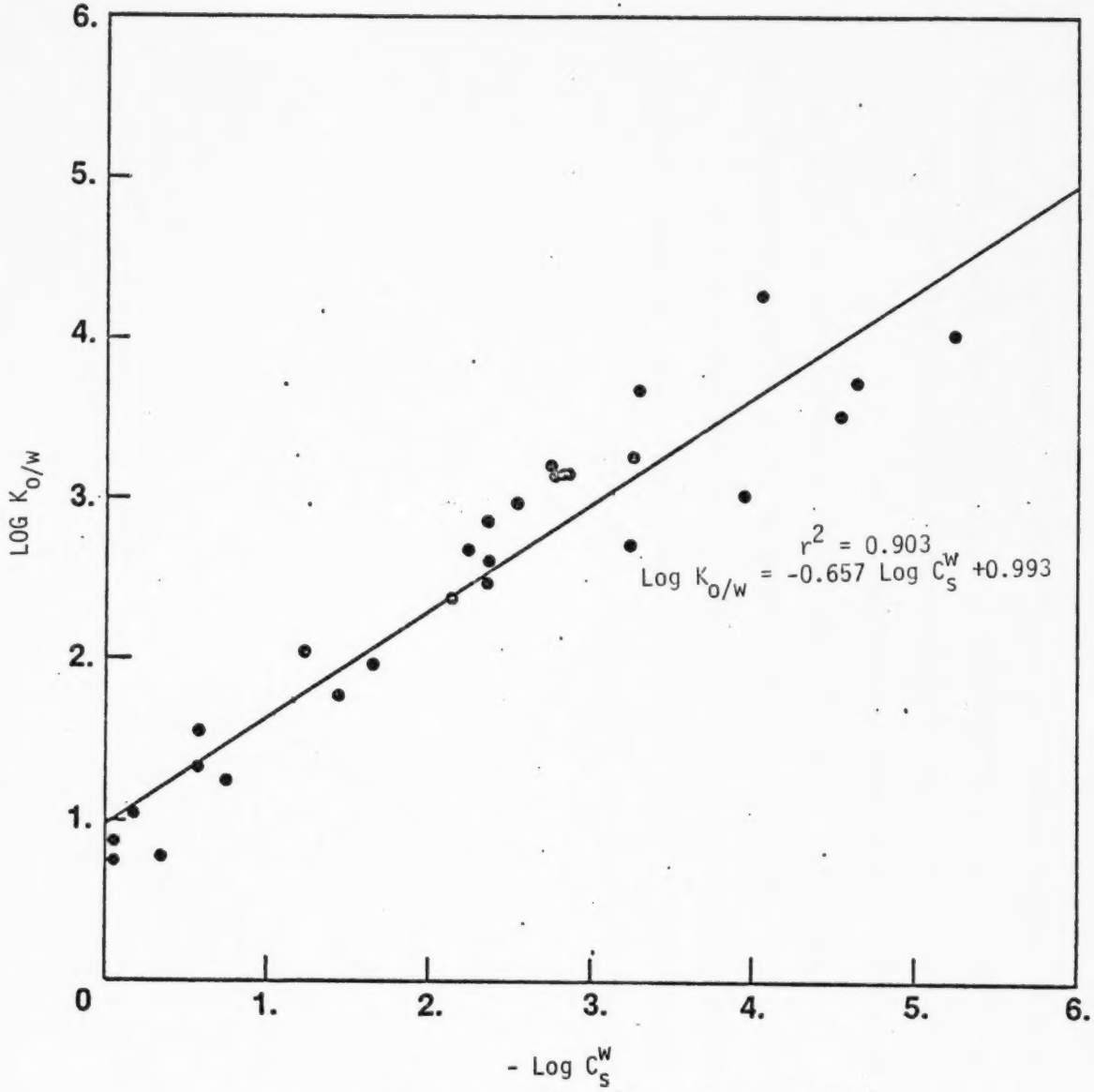

Figure 6. Log $K_{O/W}$ Versus -Log C_S^W for the Literature Values.

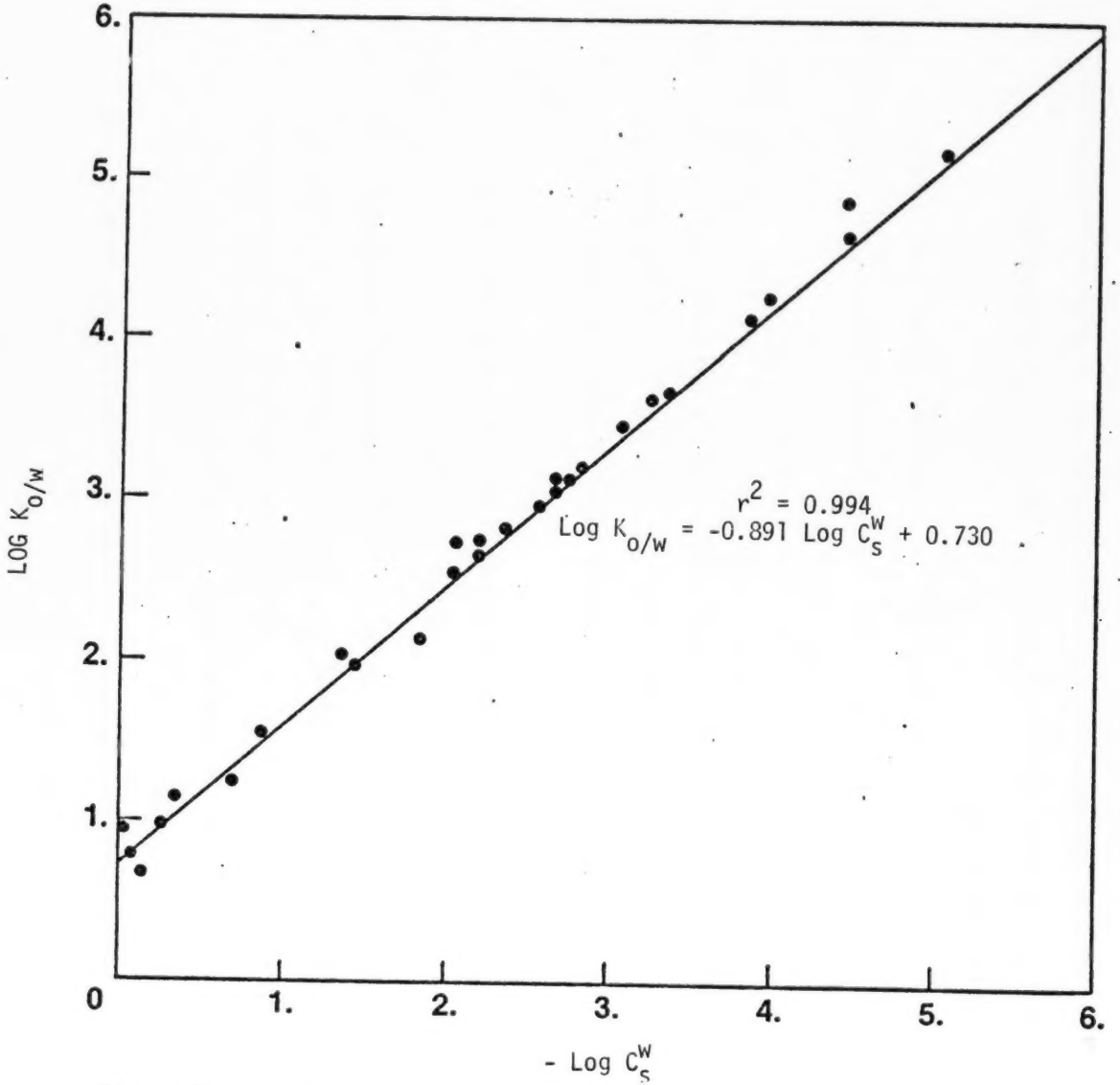

Figure 7. Log $K_{o/w}$ Versus -Log C_s^w for the experimental Values.

VII. RECOMMENDATIONS FOR FUTURE RESEARCH

In any research endeavor it is frequently the case that more new questions are asked than old ones answered. This is the case for this work. Two studies were initiated that are incomplete: (1) salinity dependence of $K_{o/w}$ and C_w and (2) the temperature dependence of $K_{o/w}$ and C_w. Information obtainted from these studies is important for determining the rate and transport of organic substances in the environment.

Salinity Dependence

It can be shown from thermodynamics that the octanol/salt water partition coefficient $K_{o/sw}$ is related to the concentration of the aqueous salt solution, C_s, by equation 1:

$$\log K_{o/sw} = \log K_{o/w} + k_s C_s \qquad (1)$$

where k_s is the salting out coefficient which is characteristic of the solute.

Thermodynamics also shows that for compounds of similar chemical structure k_s is related to the solute molar volume ∇ by equation 2:

$$k_s = k_1 + k_2 \nabla \qquad (2)$$

where k_1 and k_2 are series constants. Combining equations 1 and 2

$$\log K_{o/sw} = \log K_{o/w} + (k_1 + k_2 \nabla) C_s \qquad (3)$$

To date we have data on two different classes of compounds, the n-alcohols and the alkylbenzenes. These data were taken in order to test equation 3. It would be desirable to have data on other types of compounds in order to generalize equation 3.

Temperature Dependence

The temperature dependence of aqueous solubility may be expressed as

$$d \log C_s^w / d(1/T) = - \frac{\Delta H_s}{R}$$

ΔH_s is the heat of solution, and R is gas constant. Very little is known

about the heats of solution of hydrophobic substances. Since water temperature varies from -40°C (in the artic) to 40°C (near the equator), it is desirable to study temperature dependence in order to make accurate predictions of the aqueous solubility of organic compounds.

Head-Space Measurements

During the course of this work it was realized that it would be desirable to have another method (other than shake-flask) for measuring $K_{o/w}$ for volatile polar compounds. The shake-flask method gives unreliable results because of the relative large solubility of water in these compounds. The head-space method for determining $K_{o/w}$ [Brinckman and Bellama, 1978] avoids these experimental errors because there is no solute-water interface in these measurements. These results should be very helpful in the development of a reliable predictive scheme.

Tests for Other Classes

Additional reliable data on monofunctional groups should be generated to develop a sound prediction scheme. Compounds containing multifunctional groups should be studied and the results analyzed using additivity rules for functional groups to assess the effects of steric hindrance. Also, the aqueous solubility of organic mixtures should be studied in order to develop a sound predictive scheme for mixtures.

MacKay et al. [1980] have developed an equation which may be used to predict the aqueous solubility and octanol/water partition coefficient of rigid (solid) molecules. However, predictions are generally poor. Here our study will generate data for rigid and flexible molecules in the solid state and will develop suitable expressions to explain their aqueous solubilities.

In the study just completed, there was an attempt to choose compounds to represent a wide selection of chemical types which would be of environmental interest. Unfortunately one important group of chemicals

was left out, the organometals [Brinckman and Bellama, 1978]. The occurrence of these compounds in water is known to cause sickness and deaths. It is, therefore, desirable to determine the aqueous solubility and octanol/water partition coefficient for this class of compounds.

This study will, of course, include other classes of compounds of immediate interest to EPA.

Predictive Schemes

Success of a predictive scheme depends crucially on the accuracy of the limited experimental data on which the calculations must rest. Hansch et al. [1968] have developed a predictive scheme based on group contributions. However, there has been some concern on their reported π values. Here our goal will be to develop a more comprehensive predictive scheme. This is based on the experimental results obtained in this laboratory and should also include data on compounds containing multifunctional groups that have not been measured to date. $K_{o/w}$ and C_s^w measurements should be made on compounds containing multifunctional groups that have obvious steric hinderence. $K_{o/w}$ measurements should be taken on compounds of increasing complexity in order to determine where the group additivity breaks down.

Using thermodynamics and a simple model, log $K_{o/w}$ and log C_s^w will be related to some simple physical properties (such as, solute molar volumes, boiling points, and carbon numbers). Our preliminary study suggests that log $K_{o/w}$ and log C_s^w may be correlated to the solute molar volumes.

Organic pollutants are often multicomponent mixtures. It is, therefore, desirable to develop thermodynamic relations which can predict the aqueous solubility of each component in the mixture. These will be modeled on hydrocarbon-hydrocarbon systems but may be used to predict the solubility of complex mixtures such as DDT-kerosene systems.

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APPENDIX I

The octanol/water partion coefficient, $K_{o/w}$, is defined as the ratio of molar concentration of solute s in octanol saturated with water, C_s^o, to its concentration in water saturated with octanol, C_s^w, under equilibrium condition in an octanol/water system:

$$K_{o/w} = C_s^o / C_s^w \tag{1}$$

Furthermore, the chemical potential of the solute in water, μ_s^w, and in octanol, μ_s^o, may be expressed by the following equations:

$$\mu_s^w = \mu_s^* + RT \ln \gamma_s^w \cdot \phi_s^w \tag{2}$$

$$\mu_s^o = \mu_s^* + RT \ln \gamma_s^o \cdot \phi_s^o \tag{3}$$

where μ_s^* is the chemical potential of pure solute, R is the gas constant, T is the temperature of the system in Kelvin, ϕ_s^w and ϕ_s^o are, respectively, the volume fraction of solute in water and in octanol, and γ_s^w and γ_s^o are the solute activity coefficients on a volume fraction basis, where γ_s approaches unity as ϕ_s approaches unity, in water and in octanol, respectively.

Under equilibrium condition, $\mu_s^w = \mu_s^o$, hence

$$\gamma_s^w \phi_s^w = \gamma_s^o \phi_s^o \tag{4}$$

Similarly for a solute in equilibrium with its aqueous solution ($\mu_s^w = \mu_s^s$) the activity coefficient may also be expressed as

$$\gamma_s^w \phi_s^w = \gamma_s^s \phi_s^s \tag{5}$$

where γ_s^s and ϕ_s^s are, respectively, the solute activity coefficient and volume fraction in solute. For a solute of low aqueous solubility γ_s^s

approaches unity as ϕ_s^s approaches unity, hence

$$\gamma_s^w \phi_s^w = 1$$

or $$\gamma_s^w = (\phi_s^w)^{-1} \quad (6)$$

At infinite dilution solute concentration in aqueous phase (C_s^w) and in octanol phase (C_s^o) may be expressed by the following equations

$$C_s^w = \phi_s^w / \nabla_s^w$$

and $$C_s^o = \phi_s^o / \nabla_s^o \quad (7)$$

where ∇_s^w and ∇_s^o are, respectively, the solute partial molar volume in water and in octanol.

Combining equations 1, 4, and 7 we get

$$K_{o/w} = \frac{\gamma_s^w}{\gamma_s^o} \frac{\nabla_s^w}{V_s^o}$$

or $$\log K_{o/w} = \log \gamma_s^w - \log \gamma_s^o + \log \frac{\nabla_s^w}{\nabla_s^o} \quad (8)$$

But for all practical purposes $\nabla_s^w \cong \nabla_s^o = V_s$, the molar volume of pure solute. Hence equation (8) reduces to

$$\log K_{o/w} = \log \gamma_s^w - \log \gamma_s^o \quad (9)$$

APPENDIX II

Proposed Method for Determining Aqueous Solubility of Organic Compounds

Scope - This method covers the determination of aqueous solubility of both liquid and solid compounds. There are no restrictions on the type of compounds.

Summary of Method - Generator columns packed with a solid support and loaded with an organic substance make it possible to rapidly and conveniently equilibrate water with the organic phase by coupling the generator column to an extractor column for high pressure liquid chromatographic analysis of the aqueous solution. Errors from surface adsorption and loss to the atmosphere are avoided. Another method for determining the solute concentration in the aqueous phase is by solvent extraction of the aqueous phase followed by gas chromatographic analysis of the solvent extract.

Apparatus

1. Generator column - Two different designs were used depending on whether the eluted aqueous phase was analyzed by HPLC (Procedure A) or by solvent extraction followed by GC analysis of solvent extract (Procedure B).

The design of the generator column for procedure A is shown in Figure II-1. The column consists of a 1/4-inch O.D. Pyrex tube joined to a short enlarged section of 9mm Pyrex tubing which in turn is connected to another section of 1/4-inch O.D. Pyrex tubing. Connections to inlet Teflon tubing (1/8-inch O.D.) and to outlet stainless steel tubing (1/16-inch O.D.) are by means of stainless steel fittings with Teflon ferrules.

2. Constant temperature bath with circulation pump-bath should be capable of controlling temperature to $\pm$ 0.05°C.

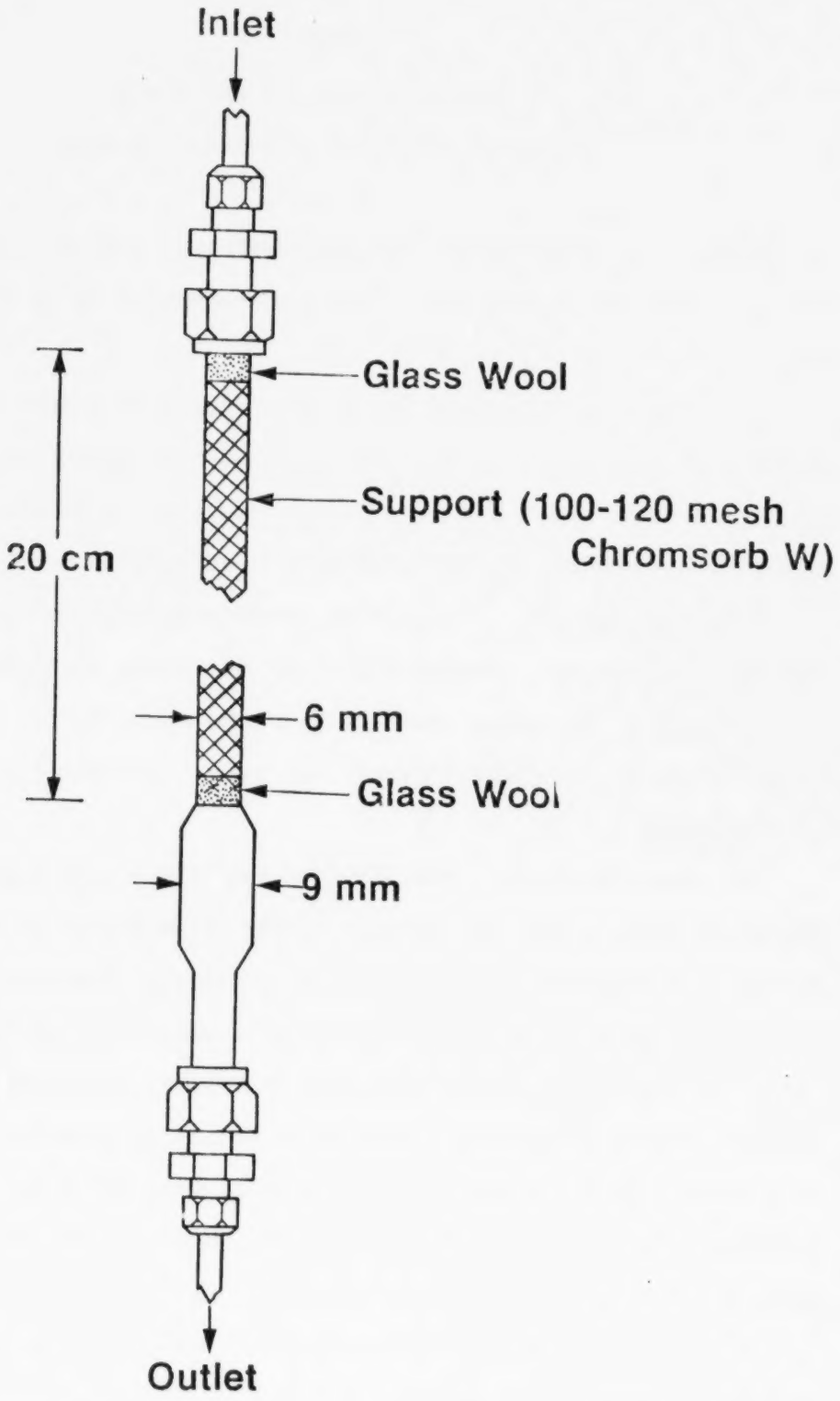

Figure II-1 Generator column.

3. High pressure liquid chromatograph equipped with a UV detector.

4. Extractor column - 6.6 X 0.6 cm stainless steel tube with end fittings containing 5 μm frits filled with a superficially porous phase packing (Bondapack C_{18}/corasil Waters Associates).

5. Two 6-port high pressure rotary valves.

6. The design of the generator column for procedure B is shown in Figure II-2. The column consists of a 1/4-inch Pyrex tube jointed to a short enlarged enlarged section of 9mm O.D. Pyrex tubing. The outlet end of the 9mm O.D. tubing is connected to a long section of 3mm O.D. stainless steel tubing. The column is enclosed in a water jacket for temperature control.

7. Collecting tube for procedure B (Figure II-2) - 8 X 3/4 inch section of Pyrex tubing with a flat bottom is connected to a short section of 3/8-inch O.D. Pyrex tubing. The collecting tube is sealed with a 3/8-inch Teflon cap fitting.

8. Gas chromatograph with hydrogen flame detector.

Procedure A - HPLC Method

Procedure A covers the determination of the aqueous solubility of compounds which absorb in the U.V. The HPLC analytical system is shown schematically in Figure II-3. Two reciprocating piston pumps deliver the mobile phase (water or methanol-water mixture) through two 6-port high pressure rotary valves and a 30 X 0.6 cm C-18 analytical column to an ultraviolet adsorption detector operating at 254 nm. Chromatogram peaks are recorded and integrated with a recording integrator.

1. Determination of response factor

   a. Prepare known concentrations (mole/L (M)) solute in methanol (standard solution).

   b. Inject samples of standard solution into HPLC system using a calibrated sample loop.

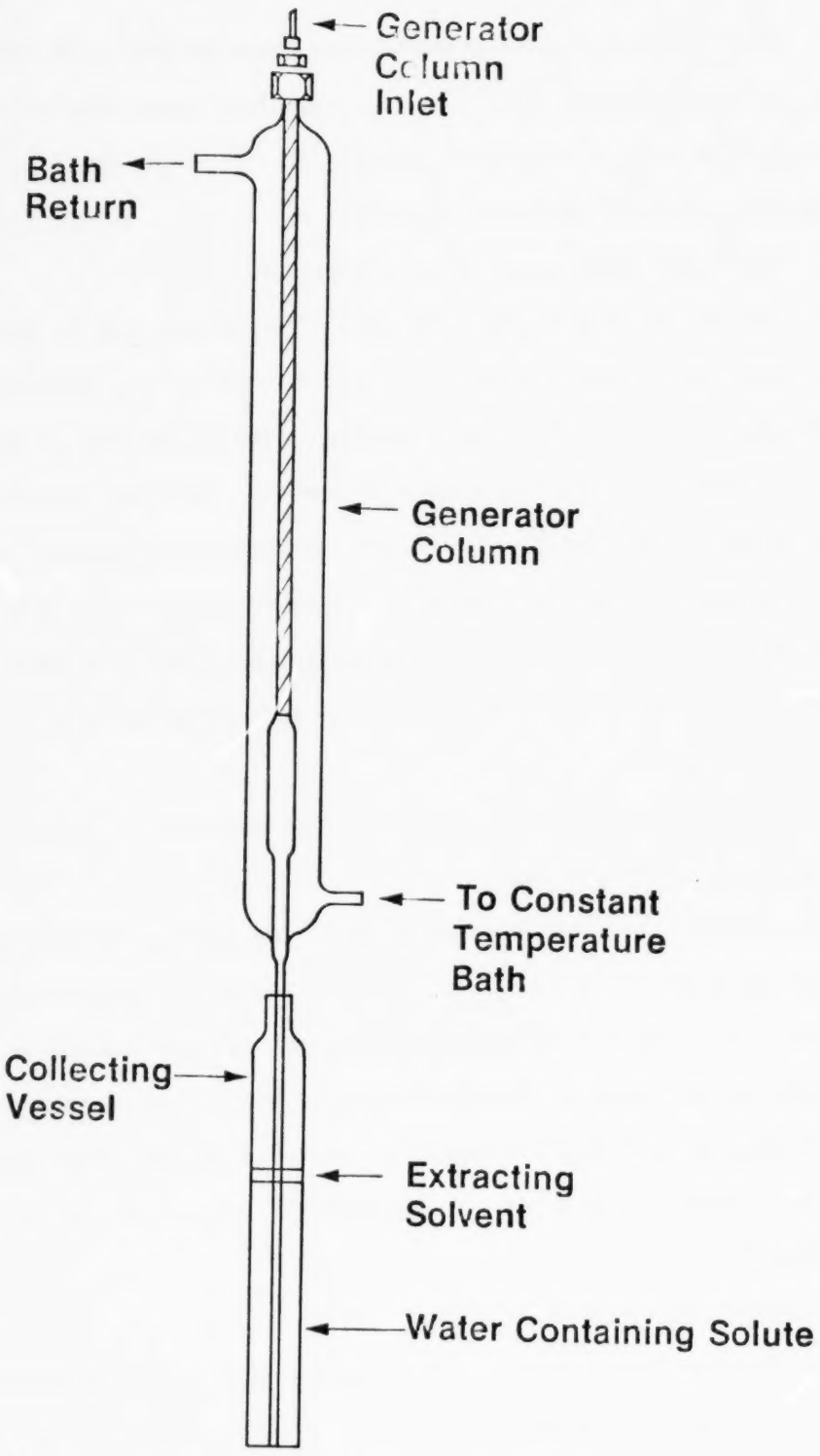

Figure II-2 Design of generator column for GC method.

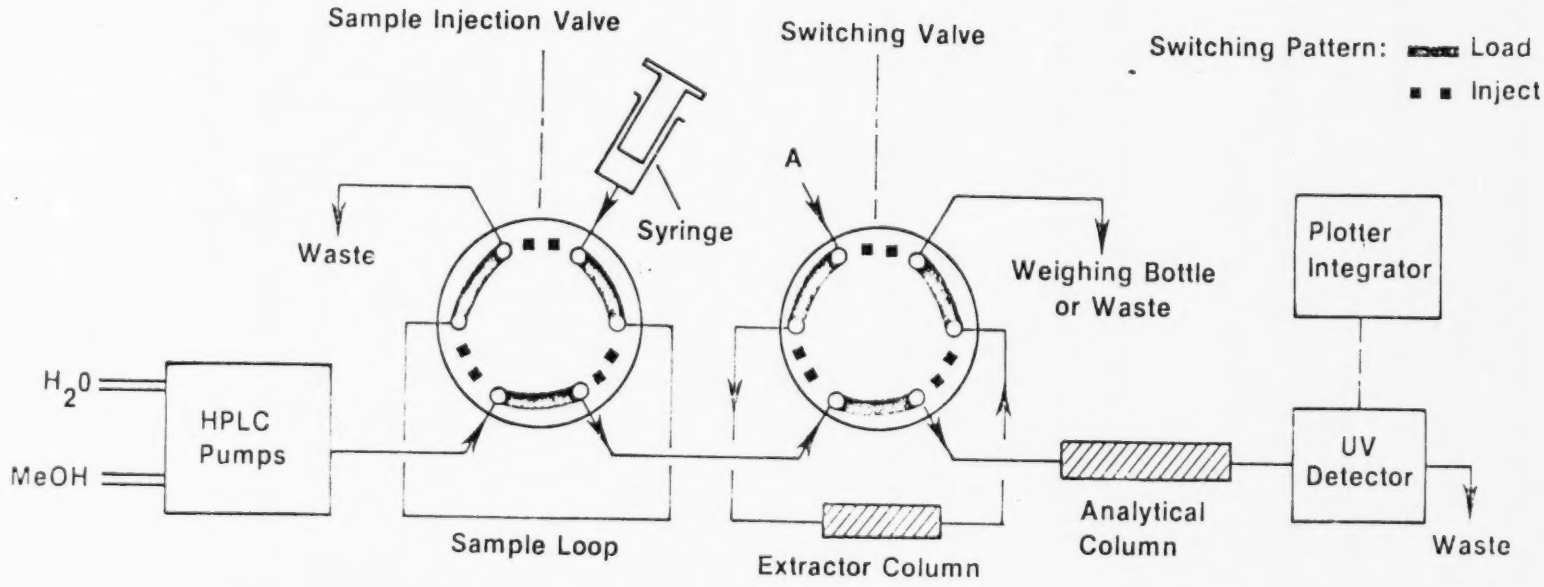

Figure II-3 Schematic of HPLC - generator column flow system.

c. Adjust organic solvent (methanol)/water ratio to obtain a reasonable retention time for solute peak.

d. Obtain an average peak area for several injections of standard sample at a set absorbance unit full scale (AUFS).

e. Calculate response factor from following equation:

$$RF = (\text{conc.}(M))\ (\text{average area})(AUFS)$$

2. Loading of Generator Column

a. The design of the generator column is shown in Figure II-1. The column consists of a 6mm of Pyrex tube jointed to a short enlarged section of 9mm Pyrex tubing.

b. To pack the column a plug of silanized glass wool is inserted into one end of the 6mm Pyrex tubing. Silanized diatomaceous silica support (about 0.5g 100-120 mesh chromosorb W cleaned by Soxhlet extraction with ethanol and dried) is poured into the tube with tapping and retained with a second plug of silanized glass wool.

c. If the solute is a liquid, the column is loaded by pulling the liquid solute through the dry support with gentle section. If the solute is a solid, a 1% solution of the solid in a volatile solvent is added to the dry packing. The solvent is then distilled off the column under reduced pressure.

3. Analysis of Solute

a. Pump water to the generator column by means of a minipump.

b. With the switching valve (Figure II-3) in the inject position, pump water through the generator column at a flow rate of 1 ml/min for approximately 5 minutes.

c. Switch HPLC pump to 100% water.

d. Weigh a 25 mL weighing bottle.

e. Once the water reaches the HPLC detector which is indicated by a negative reading on the detector, simultaneously place the weighing bottle at the waste position and turn the switching valve to the load position.

f. Switch HPLC pump back to organic (methanol)/water mixture.

g. After collecting approximately 10 mL of water in weighing bottle turn the switching valve back to inject position.

h. Replace the weighing bottle with the waste container.

i. Turn on the integrator.

j. Weigh the weighing bottle containing water sample.

k. Determine average area/g. of water collected at a selected AUFS setting from several collections.

l. Calculate the solute concentration in water by the following equation:

solute concentration (M) = (RF) (average area/g)(AUFS)(997g/L) (volume of sample loop in L)

Procedure B - GC Method

1. Determination of Calibration Curve

a. Prepare solute standard solutions of varying concentrations

b. Select a column and optimum GC operating conditions for suitable resolution between the solute and solvent and the solute and extracting solvent.

c. Inject a known volume of each standard solution into injecton part of GC.

d. Determine average area/μl for each standard solution.

e. Determine linear regression equation of concentration vs area/μl for in the following form

$$\text{conc(M)} = a \frac{\text{area}}{\mu l} + b$$

2. Loading of Generator Column

   a. Generator column is packed and loaded with solute in the same manner as for the HPLC method.

   b. Approximately 20 cm of straight stainless steel tubing is connected to the bottom of the generator column and a beaker is placed beneath the tubing to collect the water.

   c. The top of the generator column is connected to a water reservoir (Figure II-4) using Teflon tubing.

   d. Air or nitrogen pressure (5 P.S.I.) from an air or nitrogen cylinder is applied to the water reservoir thus forcing water from the reservoir through the column to the beaker.

   e. Water is collected in the beaker for approximately 10 min. while the solute concentration in water equilibrates.

3. Collection and Extraction of the Solute

   a. During the equilibration time, a known weight of extracting solvent is added to a collection vessel which contains a glass-enclosed stirring rod and can be capped. The extracting solvent should completely cover the bottom of the collection vessel.

   b. Record the weight of collection vessel with cap and extracting solvent.

   c. Remove the cap from the collection vessel and place it under the generator column so that water from the generator column enters below the level of the extracting solvent (Figure II-2).

   d. When the collection vessel is filled, remove it from under the generator column, replace the cap, and weigh the filled vessel.

   e. Determine the weight of water collected.

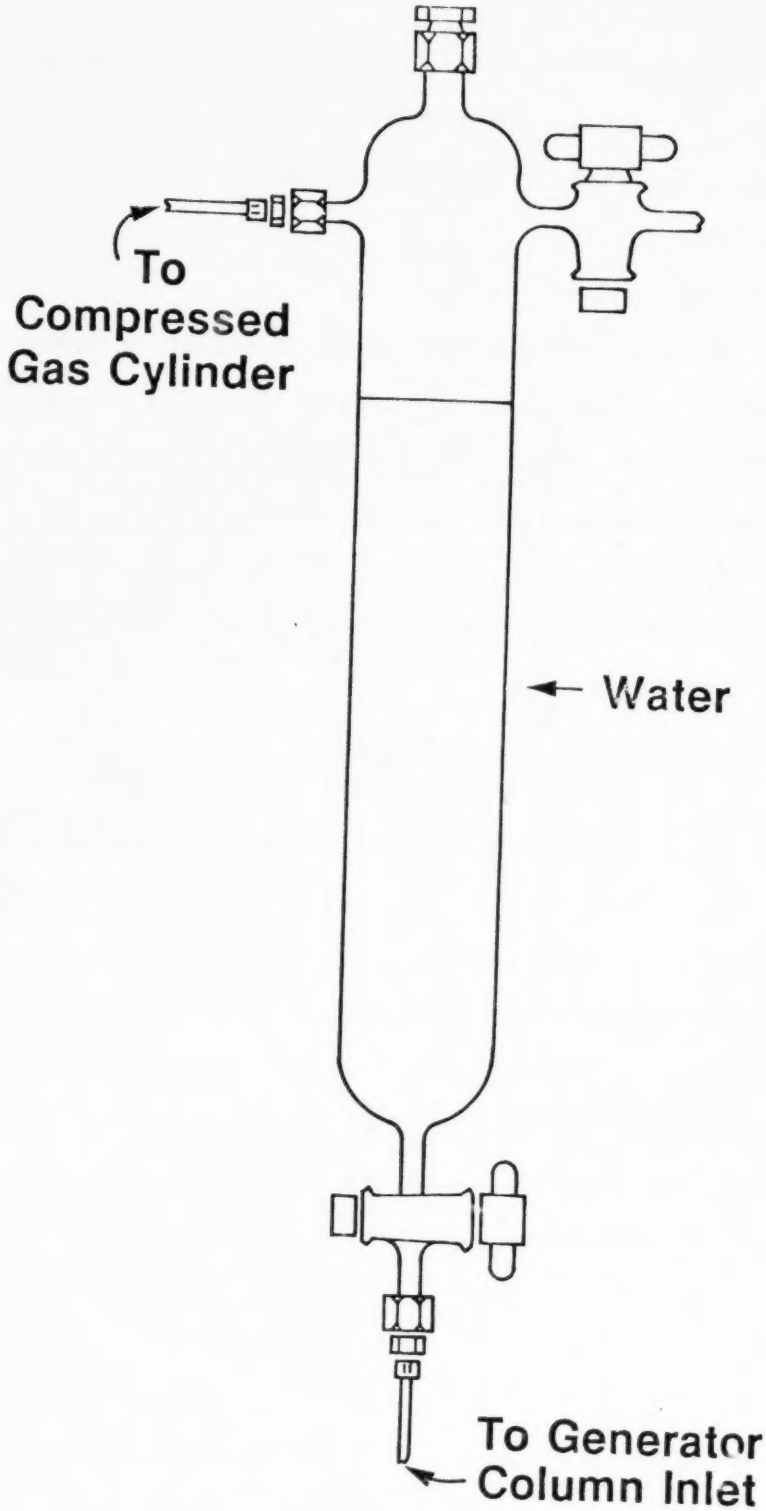

Figure II-4 Water reservoir for GC method.

f. Place the collection vessel on a magnetic stirrer and stir the contents for approximately 30 min. controlling the rate of stirring so as not to break the meniscus between the extracting solvent and water layers.

4. Analysis of the solute

a. After stirring remove a known volume of extracting solvent from the vessel using a microliter syringe and inject into the G.C.

b. Record the peak area/μL injected and from the regression equation of the calibration line, determine the concentration of solute in extracting solvent.

c. The concentration of solute in water (M), C_s^w , is determined from the following equation

$$C_s^w = \left(C_s^{es}\right)\left(\frac{d_{H_2O}}{d_{es}}\right)\left(\frac{g_{es}}{g_{H_2O}}\right)$$

where C_s^{es} is the concentration of solute in extracting solvent (M), d_{H_2O} and d_{es} are the densities of water and extracting solvent, respectively, and g_{es} and g_{H_2O} are the grams of extracting solvent and water, respectively, contained in the collection vessel.

d. Replicate injections are made from each collection vessel to determine an average concentration in water for the vessel.

e. At least one additional collection vessel is prepared in a similar manner for each generator column.